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Active

Project #: E-19-X41 Cost share #: Rev #: 2
Center # : 10/24-6-R7106-4A0 Center shr #: OCA file #:
Work type : RES
Contract#: 5 R01 HL45485-04 Mod #: DELIV SCHEDULE Document : GRANT
Prime #: Contract entity: GTRC

Subprojects ? : N CFDA: 93.837
Main project #: PE #:

Project unit: CHEM ENGR Unit code: 02.010.114
Project director(s):
YOGANATHAN A P CHEM ENGR (404)894-2849

Sponsor/division names: DHHS/PHS/NIH / NATL INSTITUTES OF HEALTH
Sponsor/division codes: 108 / 001

Award period: 940101 to 941231 (performance) 950331 (reports)

Sponsor amount	New this change	Total to date
Contract value	0.00	126,234.76
Funded	0.00	126,234.76
Cost sharing amount		0.00

Does subcontracting plan apply ?: N

Title: QUANTITATION OF VALVULAR REGURGITATION AN IN VITRO STUDY

PROJECT ADMINISTRATION DATA

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Security class (U,C,S,TS) : U ONR resident rep. is ACO (Y/N): N
Defense priority rating : NIH supplemental sheet
Equipment title vests with: Sponsor GIT X

Administrative comments -
P.I. HAS ADVISED OCA THAT GRANT RENEWAL WILL NOT BE REQUESTED, THEREFOR THE ANNUAL REPORT REQUIREMENT IS DELETED.

GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION

NOTICE OF PROJECT CLOSEOUT

Closeout Notice Date 03/20/95

Project No. E-19-X41_____ Center No. 10/24-6-R7106-4A0_

Project Director YOGANATHAN A P_____ School/Lab CHEM ENGR_____

Sponsor DHHS/PHS/NIH/NATL INSTITUTES OF HEALTH_____

Contract/Grant No. 5 R01 HL45485-04_____ Contract Entity GTRC

Prime Contract No. _____

Title QUANTITATION OF VALVULAR REGURGITATION AN IN VITRO STUDY_____

Effective Completion Date 941231 (Performance) 950331 (Reports)

Closeout Actions Required:	Y/N	Date Submitted
Final Invoice or Copy of Final Invoice	Y	_____
Final Report of Inventions and/or Subcontracts	Y	_____
Government Property Inventory & Related Certificate	N	_____
Classified Material Certificate	N	_____
Release and Assignment	N	_____
Other _____	N	_____

Comments_____
USE DHHS FORM FOR PATENT_____

Subproject Under Main Project No. _____

Continues Project No. _____

Distribution Required:

Project Director	Y
Administrative Network Representative	Y
GTRI Accounting/Grants and Contracts	Y
Procurement/Supply Services	Y
Research Property Managment	Y
Research Security Services	N
Reports Coordinator (OCA)	Y
GTRC	Y
Project File	Y
Other _____	N
_____	N

NOTE: Final Patent Questionnaire sent to PDPI.

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Regents Professor Ajit P. Yoganathan
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March 13, 1995

Ms. Carol Dangel
NIH / NHLBI-DEA
Westwood Building, Room 4A11
5333 Westbard Ave.
Bethesda, MD 20892

Dear Ms. Dangel:

Enclosed are three copies of my final report for grant HL#45485. In addition to a summary of the technical accomplishments, a list of **peer reviewed publications** resulting from the work funded by the grant is also included If you need any further information please contact my office.

Sincerely,

Ajit P. Yoganathan, Ph.D.
Regents Professor, Chemical & Mechanical Engineering
Co-Director Bioengineering & Emory/GaTech Biomedical Technology Centers

APY/bcc

cc: Faith Gleason - OCA
Claudia Clarkson - CHE

FINAL REPORT TO NIH (GRANT # HL 45485)

QUANTITATION OF VALVULAR REGURGITATION: AN IN VITRO STUDY

Principal Investigator: Professor Ajit P. Yoganathan
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1. Specific Aims of Original Proposal

The goals of this proposal are three-fold. **First**, the study will address the hypothesis that equations can be derived from basic fluid mechanic principles to quantify regurgitant volume using quantities that can be directly measured by Doppler. **Second**, these basic physical principles can be used to interpret color flow mapping variability related to regurgitant jet behavior in the presence of solid structures in interrupting flows. **Third**, additional variability inherent to measurement technique (i.e. instrument settings) will be addressed.

To achieve these objectives, the following specific aims are proposed: 1) to derive equations from the principles of turbulent jet flow and conservation of mass which provide orifice flow rate, and therefore regurgitant volume, as a function of Doppler measurable quantities; 2) in *in vitro* models, to test the accuracy of the equations in predicting actual regurgitant volume; 3) to define an *in vitro* model, the relationship between regurgitant flow, and spatial characteristics of the color flow jet, namely, jet length, width, area, and volume; 4) in *in vitro* models, to address the variability in these relationships due to machine settings, driving pressure, and physiologically observed jet flow phenomena, namely, the Coanda effect, impingement, counterflow, and coflow; and 5) to investigate the applicability of the quantitation techniques to various designs of heart valve prostheses.

These comprehensive studies are performed *in vitro* in order to allow precise and independent control of all variables. *In vitro* studies, while providing realistic environments, do not generally allow independent control of variables such as is required for such fundamental studies. Careful design of flow models provides semi-realistic environments, while allowing dependent control.

2. Studies and Results

A. CONSERVATION OF MOMENTUM TECHNIQUE APPLIED TO REGURGITANT JETS

The purpose of this study was to determine whether the inverse relationship of centerline velocity to distance develops sufficiently rapidly so that quantitative techniques based on that decay would be applicable over a wide range of heart rates. Two different techniques, an engineering tool, laser Doppler anemometry, and a clinical tool, Doppler ultrasound, were used for measuring jet centerline velocities (averaged over multiple beats). Physiologic pulsatile flows were pumped through two circular orifices, 4 and 6 mm in diameter, at 60 to 150 beats/min; peak orifice velocities ranged from 2 to 5 m/sec. Steady flow experiments were also performed with the same orifice diameters and over the same velocity range. Peak centerline velocities in the fully developed turbulent jet region decayed inversely with distance at all heart rates studies. With laser Doppler anemometry, the proportionality constant of the decay curve was found to be in the range 6.4 ± 0.5. The pulsed Doppler results provided a jet constant in the range 6.7 ± 0.3 with the 4-mm orifice diameter, whereas the constant was 6.5 ± 0.3 with the 6-mm orifice diameter. In steady flow, the proportionality constant was found to be 6.1 ± 0.2. Therefore, within a ride range of physiologic heart rates, full jet development occurs with sufficient speed so that the expected centerline velocity decay is established (jet empirical constant of 6.3). The conservation of momentum technique for calculating orifice flow rate on the basis of these centerline velocities is thus applicable under physiologic conditions.

B. EFFECTS OF CONFINED AND IMPINGING REGURGITANT JETS

Methods have recently been developed for noninvasive quantification of valvular regurgitant flow rate (Q_{op}) based on conservation of momentum within free turbulent jets and

the resulting decay of peak centerline velocities (U_{mp}) distal to the orifice. Before clinical implementation, however, the method must account for realistic environments in which jets are limited axially (impinging on distal walls), confined laterally or both, causing more rapid velocity decay. We proposed that accurate results could be achieved for such jets using a technique based on the continuity principle coupled with a dimensional analysis involving factory affecting U_{mp}: receiving chamber diameter (D_C) orifice-to-end wall distance (H), distance from the orifice, peak orifice velocity (U_{op}) and orifice diameter (D_O). The purpose of this study was to validate this method *in vitro*, over a wide range of heart rates (HR), U_{op}, and H. Physiologic pulsatile flows were pumped through circular orifices (D_O=2,4 mm) at 70 -150 beats/min in two receiving chambers (D_C=51, 88 mm); at each HR, U_{op} was varied from 2 - 5 m/s. H varied from 30 - 93 mm. U_{mp} was measured by pulsed Doppler ultrasound over multiple beats and Q_{op} calculated. Predicted Q_{op} agreed well with actual values by electromagnetic flow probe, independent of HR. For example, for D_C=51 mm, H= 66mm, the regression for Q_{op} was y=0.97x-0.21 (r=0.99). For D_C=51 mm, H=30 mm, the regression was y= 1.01x+0.13 (r=0.99). For a wide range of geometries confining jets axially and laterally, Q_{op} can be accurately predicted in vitro from velocities that can be directly measured by conventional Doppler.

C. INTERACTION OF SOLID BOUNDARIES WITH JETS

This study addressed the hypothesis that adjacent walls influence regurgitant jet size as seen on color Doppler flow maps. Steady flow was driven through circular orifices (0.02 to 0.05 cm^2) at physiologic velocities of 2 to 5 m/s. At a constant flow rate and orifice velocity, orifice position was varied to produce three jet geometries: free jets, jets adjacent to a horizontal chamber wall lying 1 cm below the orifice, and wall jets with the orifice at the level of the wall. Color Doppler flow imaging was performed at identical instrument settings for all jets.

In echocardiographic views perpendicular to walls (vertical views), most commonly used *in vivo* for imaging jets near cardiac structures, a jet lying along the wall appears smaller than a free jet produced by the same regurgitant flow. The wall jet can entrain fluid and expand only on one side, and it spreads laterally over the surface to a greater extent. The area of a deflected jet is increased by the Coanda effect, which draws the proximal jet towards the wall. Therefore, jet size cannot be related to the degree of regurgitation without considering jet geometry and adjacent walls.

D. EFFECTS OF INSTRUMENT SETTINGS AND TECHNICAL FACTORS

Color Doppler flow images and spectral Doppler tracings were obtained under steady flow conditions in the American Society of Echocardiography flow phantom. This flow phantom was designed in our laboratory. Measurements were taken at steady flow rates over a range of 55 to 550 cm^3/s, using a variety of clinically available ultrasound instruments (ATL UM9, Toshiba 65A, 270A, Kontron Sigma 44, Vingmed SD 100). Machine settings such as: packet size, wall filter, PRF, power function and scan line density were varied. The color images were analyzed on a MAC II ci system using software programs developed in our laboratory. the results indicate that for a given instrument, varying machine parameters has a marked effect on the visualized and the quantitative representation of the color flow image.

In addition we addressed the hypothesis that, at a constant peak flow rate, increasing heart rate could decrease the maximum apparent jet size by color flow Doppler mapping. We examined this in pulsatile flow, holding orifice size and peak flow rate constant and varying heart rate (70-180 beats/min) and frame rate (3 rates) for jets of low and high momentum (2-5 m/s). Maximum jet area was measured in 10 consecutive beats at each heart rate and frame rate, and

averaged. Increased heart rate can cause underestimation (as much as 40%) of apparent jet size by color flow mapping for a given peak flow rate, particularly for jets with low momentum and delayed penetration into the receiving chamber. This may be relevant to acute severe regurgitation with increased heart rate. This effect can be reduced by increasing frame rate, and should be considered in relating jet size to the severity of regurgitation.

A Kontron Sigma-44 color flow Doppler unit with a two-frequency transmitter (QUASAR) can potentially increase the maximum detectable velocity. We imaged tube and jet flows *in vitro*, in order to evaluate the accuracy of the QUASAR system. Centerline velocities above the unshifted Nyquist limit were corrected to nonaliased displays. The QUASAR concept is a critical step toward obtaining quantitative color Doppler flow data for the first time. The importance of obtaining such physically meaningful data is highlighted by recently reported clinical assessment techniques which rely on a limitation of status-quo color flow Doppler, namely, aliasing.

Color Doppler (CD) jet flow area (CDA) continues to be used as the primary noninvasive marker of the severity of valvular regurgitation (VR) and the transesophageal approach (TEE) has aided visualization of CDA in prosthetic valves. It has been shown that CDA varies significantly between transthoracic and TEE views within a given instrument. In order to define useful thresholds of severity of VR, it is critical to examine the variability between different instruments and between instrument settings for the same flow. This study therefore addressed the effect of instrument settings and intermachine variability in a comprehensive manner using six commonly used TEE instruments. Commercially available CD instruments by Acuson, Aloka, ATL, HP, Toshiba and VingMed with 5 MHz transesophageal probes were used to image pulsatile jet flow through a 5 mm orifice using a blood analog fluid. For all six machines studied, a reduction in Nyquist Limit (0.46 - 0.32 m/s) resulted in an increase in CDA (8.82-18.10 cm^2) ($p=0.001$). Nyquist limit should not in principle affect CDA, and these changes are explained by changes in wall filter. With other settings constant, increasing sector angle (45°-90°) produced larger jets (13.23 - 18.44 cm^2) due to lateral resolutions effects ($p=0.01$). Virtually identical setting combinations showed intermachine differences as high as 57%. Instrument settings cause significant variations in CDA for constant flow conditions and so must be annotated and recorded. Limited setting choices and arbitrary annotation prohibits extrapolation of assessment techniques between instruments.

E. EFFECT OF COUNTER AND CO-FLOWS ON REGURGITANT JETS

The purpose of this study was to address the hypothesis that physiologic counterflow field may influence regurgitant jet size. Steady flow was driven through 0.02-.12cm^2 circular orifices at .5-5 m/s. At a constant orifice velocity and flow rate, the velocity of a uniform counterflow field was varied from 1 to 8 cm/s. Jet penetration length was measured by fluorescent dye visualization in 10 video frames to average out turbulent fluctuations. Despite its relatively low velocities, counterflow dramatically curtailed jet length. For example, the length of a 1.8 m/s jet (.05 cm^2 orifice) decreased from 20 to 10 cm as counterflow velocity increased from 3 to 7.5 cm/s. Jet length decreased as the ratio of counterflow to jet momentum increased, but with a nonlinear relationship: length declined steeply for low-momentum jets (momentum ratio < 1.0) and with a more shallow slope for high-momentum jets (ratio > 1.0). Counterflow fields analogous to atrial inflow have an important effect on the length of regurgitant jets. Low-momentum jets, such as TR, are move sensitive to counterflow, while high-momentum jets, such as significant MR, are less sensitive. Further studies have also shown that wall jets in a counterflow are uniformly longer than center jets (up to 40% longer for jets of high momentum).

F. COMPUTER SIMULATION STUDIES

To rigorously explore factors affecting jet size, a computer model was developed which simulates color Doppler jets for user inputs of lesion velocity, orifice velocity, orifice area, chamber depth, transducer depth and instrument settings. The software is easily used for a full range of physiologic conditions for all four cardiac valves. Animation of the output on a Silicon Graphics workstation enhances the user's ability to visualize changes in color Doppler images for different physiologic inputs. The results using this model in our laboratory have shown immediate clinical relevance about factors affecting jet size to an extent no possible, *in vitro* or *in vivo*.

Recent computational studies have shown that the proximal isovelocity surface area (PISA) method can quantify valvular regurgitation. The purpose of this study was to determine whether it could be applied accurately in the presence of ventricular outflow, which can distort the PISA field. Finite difference solution of the Navier-Stokes equations was therefore performed in an anatomically correct 3-dimensional ventricular model. Flow was driven through 4-6 mm diameter regurgitant orifices by a 100 mmHg pressure gradient. Each orifice size was located centrally, or near the outflow tract or posterior wall.

Regurgitant flow rates (Q) ranged from 41 to 101 ml/s. For each aliasing velocity (V) and PISA radius (R) along the centerline of the orifice, the flow rate as calculated by $Qc=2\pi R^2V$. To account for underestimation near the orifice and overestimation far from it (finite chamber and outflow effects), a polynomial was fitted to plots of Qc vs. R, and Qc at the point of inflection taken as the best estimate of actual Q (least distortion). Qc at the point of inflection agreed well with actual values (mean error = 4.3 ml/s, or 6.1%), successfully accounting for potential overestimation, particularly nearest the outflow. This computational study confirms that ventricular outflow can distort adjacent PISAs, but that flow rate can still be calculated accurately by analysis of the proximal flow field in a way that could potentially be automated.

Systolic pulmonary venous (PV) flow is primarily determined by atrial pressure events. As the atrium relaxes, atrial pressure decreases and creates a favorable gradient for forward systolic flow into the atrium. However, the additional volume of regurgitation causes atrial pressure to increase rapidly and creates a pressure gradient favoring flow out of the atrium (PV flow reversal). Since the rise in pressure due to additional volume is determined by atrial compliance, we tested the hypothesis that the presence and magnitude of flow reversal is not only a function of regurgitant volume but depends on atrial compliance as well. A mathematical model of an atrium with varying compliance and PVs was developed. The atrial pressure-volume (compliance) relationship was modeled as an exponential function: initially rapidly increasing compliance (atrial relaxation) which then decreased as atrial volume increased. A simplification of the Navier-Stokes fluid flow equations was used to solve for PV velocities that result from the developed pressure gradient. Using an initial atrial volume of 40 cc (normal), the modeling was performed over a range of initial atrial compliances (C = 3-10 cc/mmHg), with and without the addition of a regurgitant jet. The model realistically simulated the systolic PV wave form in magnitude and morphology. As the volume of regurgitation increased, peak flow velocity decreased, and eventually late systolic flow reversal occurred. However, the presence and magnitude of flow reversal was determined by atrial compliance. As the initial atrial compliance decreased, the magnitude of flow reversal increased, because higher atrial pressures were developed and promoted flow out of the atrium into the PVs. PV flow reversal depends on atrial compliance as well as regurgitant volume. As initial atrial compliance decreases (stiffer atria), the likelihood of flow reversal increases. As a result, flow reversal is more likely in acute compared to chronic regurgitation because the atrium is less compliant.

G. PROSTHETIC VALVE STUDIES

A theoretical treatment using turbulent jet theory has yielded a new equation for predicting regurgitant flow through bileaflet heart valve prostheses, the most commonly implanted mechanical valve design. Previously reported techniques assuming an axisymmetric jet are not applicable to the slot-like orifices presented in these valves. The equations were therefore re-derived in the context of the prosthetic valve geometry. The purpose of this study was to develop such a method and demonstrate its applicability in principle by using in vitro models. The method was validated under both steady and pulsatile flow conditions. Having derived a method geometrically specific to the slot-like orifices presented in bileaflet mechanical heart valves, it should be applicable from patient to patient due to the rigid nature of the valve. These idealized in vitro studies, along with the accompanying theoretical derivation, will guide implementation in the clinical setting.

H. PROXIMAL FLOW CONVERGENCE STUDIES

Recent studies have shown that the flow convergence region proximal to an orifice can be used to quantify flow rate by Doppler flow mapping. clinically, however, flow may converge toward aortic or mitral regurgitant orifices over a 3-dimensional (3D) or conical angle. Therefore, we tested the hypothesis that calculating orifice flow rate requires that the 3D angle of approach be taken into account. Steady flow (1-3 l/min) was pumped through circular orifices in an upright and inverted 90° cone and flow rate was calculated with and without the 3D angle factor. Flow ± 4% for the upright cone and overestimated them by 230 ± 26% for the inverted cone. Correcting for the 3D angle gave values within 5% of actual ones (r=.98, SEE=.13 l/min). Application of the proximal convergence method for flow through restrictive orifices must take into account the three-dimensional angle determined by the surrounding leaflets.

The effect of aortic outflow on the quantification of mitral regurgitation using the flow convergence method was investigated by both in-vitro experiments and computational simulations. Digital analysis of the color Doppler M-mode images were compared to results obtained using laser Doppler anemometry, an engineering gold standard and three-dimensional computational simulations. Regurgitant orifices of 3.2 and 6.4 mm in diameter were used with aortic flow rates from 0 L/min to 30 L/min. In the absence of aortic outflow, a clear plateau was observed in plots of the calculated flow rate as a function of the distance from the orifice, indicating that there was a zone where the hemispheric assumption was valid. As the aortic outflow was increased, the length of this plateau region decreased, and then disappeared at high aortic flow rates. Further from the orifice, beyond the plateau zone, the flow rate was overestimated and this overestimation increased with increasing aortic flow rate. Results showed excellent agreement between in-vitro experiments and computational simulations. This study demonstrated that aortic outflow has a dramatic effect on the flow convergence region, and therefore must be considered in flow rate calculations.

I. EFFECT OF VALVULAR MOTION ON QUANTIFICATION OF REGURGITATION

This study addressed the hypothesis that motion of the surface containing a regurgitant orifice relative to the Doppler ultrasound transducer can cause differences between actual flow rate and calculations based on the proximal flow convergence technique. In vitro studies quantitating regurgitant flow rate by proximal flow convergence have been limited to stationary orifices. Clinically, however, valve leaflets generally move relative to the ultrasound transducer during the cardiac cycle, and can move at velocities important relative to the measured color aliasing velocities. The transducer therefore senses the vector sum of actual flow velocity toward the orifice and orifice velocity relative to the transducer. This can cause potential over- or underestimation of true flow rate depending on the direction of surface motion. The hypothesis

was explored computationally an tested by pumping fluid at a constant flow rate through an orifice in a plate moving at 0-8 cm/s (velocities comparable to those described clinically for mitral and tricuspid annular motion toward an apical transducer).

Surface motion in the same direction as flow caused overestimation of the aliasing radius and calculated flow rate. Surface motion opposite to the direction of flow (typical for mitral and tricuspid regurgitation viewed from the apex or esophagus) caused underestimation of actual flow rate; the underestimation was greater for lower aliasing velocities (36 ± 11% for 10 cm/s versus 23 ± 6% for 20 cm/s). Correcting for surface motion provided excellent agreement with actual values ($y = 0.97x + 0.10$, $r = 0.99$, SEE = 0.17 l/min). Physiologic motion of the surface containing a regurgitant orifice can cause substantial differences between actual flow rate and that calculated by the proximal flow convergence technique. Low aliasing velocities used to optimize that technique can magnify this effect. Such errors can be minimized by using higher aliasing velocities (compatible with the need to measure the aliasing radius) or eliminated by correcting for surface velocity determined by an M-mode ultrasound scan.

J. CONTROL VOLUME METHOD

The object of this work was to develop a new method to measure heart valvular regurgitation based on control volume theory and to verify it's accuracy in-vitro. Current methods to quantify valvular regurgitation rely too much on assumptions about the flow field and are therefore difficult to apply in-vivo. In particular the PISA method oversimplifies the proximal velocity field by assuming hemispherical isovelocity contours proximal to the orifice. This severely limits the applicability of the PISA method. Using basic control volume theory however removes the need to assume the manner in which the proximal flow accelerates towards the regurgitant orifice, the shape and size of the orifice, the shape of the orifice plate and the non-Newtonian behavior of the fluid. Apart from a correction that is necessary if the orifice plate is moving, this method only assumes the incompressibility of the fluid and is therefore a potentially more accurate approach. In addition, the use of magnetic resonance precludes the need for an acoustic window.

Magnetic resonance has been used to measure the three dimensional velocity field proximal to regurgitant orifices including single and multiple orifices and a cone shaped orifice plate. Both steady (0 to 7.5 l/min) and pulsatile (2 and 3 l/min) flows were used. By integrating this velocity over a control volume surrounding the orifice, the flow rate through the orifice was calculated.

It was found that magnetic resonance could measure the three dimensional flow proximal to regurgitant orifices. This enabled the calculation of the flow rate through the orifice by integrating the velocity over the surface of a control volume covering the orifice. This flow rate correlated well with the actual flow rate (0.992, correlation line slope = 1.01). Care had to be taken, however, to exclude from the integration regions of aliased velocity.

This method has been shown to be very accurate in-vitro and is therefore a potentially accurate way to quantify valvular regurgitation.

K. EFFECT OF COUNTERFLOW ON REGURGITANT JETS

Recent studies have attempted to predict the severity of regurgitant lesions from color Doppler jet size, which is a function of orifice momentum for free jets. Jets of mitral and tricuspid regurgitation however, are opposed by flows entering the atria. Despite their low velocities, these counterflows may have considerable momentum that can limit jet penetration. The purpose of this study was to address the hypothesis that such counterflow fields influence regurgitant jet size. Steady flow was driven through 2.4 and 5.1 mm diameter circular orifices at

2 - 6 m/s. At a constant orifice velocity and flow rate, the velocity of a uniform counterflow field was varied from 5 to 30 cm/s. Jet dimensions were measured by both fluorescent dye visualization and Doppler color flow mapping. The results showed that despite its relatively low velocities, counterflow dramatically curtailed jet length and area. Jet dimensions were functions of the ratio of jet to counterflow momentum. Thus, atrial inflow may participate in determining jet size and can alter the relation between jet size and lesion severity in mitral and tricuspid regurgitation.

A method for quantifying mitral and tricuspid regurgitant volume that utilizes a measure of jet orifice velocity (Uo-m/s), a distal centerline velocity (Um-m/s), and the intervening distance (X-cm) was recently developed; where jet flow rate (Qc-L/min) is calculated as Qc = (UmX)2/(26.46Uo). This method, however, modeled the regurgitant jet as a free jet, whereas many atrial jets are counterflowing jets because of jet opposing intra-atrial flow fields (counterflows). This study concentrated on the feasibility of using the free jet quantification equation in the atrium where ambient flow fields may alter jet centerline velocities and reduce the accuracy of jet flow rate calculations. A 4 cm wide chamber was used to pump counterflows of 0, 4, and 22 cm/s against jets of 2.3, 4.5, and 6.4 m/s originating from a 2 mm diameter orifice. For each counterflow-jet combination, jet centerline velocities were measured using laser Doppler anemometry. Jet flow rates (Qc) were calculated as described above, compared to the known flow rate (Qo), and the accuracy (Qc/Qo) computed. For free jets (no counterflow), flow rate was calculated with 98% mean accuracy. For all jets in counterflow, the calculation was less accurate as: (i) the ratio of jet orifice velocity to counterflow velocity decreased (Uo/Uc), i.e. the counterflow was relatively more intense and (ii) centerline measurements were made further from the orifice. But although counterflow lowered jet centerline velocities beneath free jet values, it did so only significantly in the jet's distal portion (X/D > 16, i.e. greater than 16 orifice diameters from the origin of the jet). Thus, the initial portion (X/D <16) of a jet in counterflow behaved essentially as a free jet. As a result, even in significant counterflow, jet flow rate was calculated with > 93% accuracy and > 85% for jets typical of mitral and tricuspid regurgitation, respectively. Counterflow lowers jet centerline velocities beneath equivalent free jet values. This effect, however, is most significant in the distal portion of the jet. Therefore, regurgitant jets, although not classically free because of systolic atrial inflow or jet induced intra-atrial swirling flows, will decay in their initial portions as free jets and are candidates for quantification with the centerline technique.

Mitral and tricuspid regurgitation result in the formation of turbulent jets within the atria. Clinically, for the purpose of estimating regurgitant severity, jet size is assumed to be proportional to peak jet flow rate. However, the relationship is not that simple because the determinants of jet size are complex and include interactions between jet pulsatility, jet momentum, atrial width, and the velocity of ambient atrial counterflows. Using an *in vitro* simulation, these effects on fluorescent jet penetration were measured. Both steady and pulsatile jets were driven into an opposing counterflow velocity field and peak jet length (L_{jp}) was measured as a function of peak orifice velocity (U_{jp}), the time required for the jet to accelerate from zero to peak velocity (T_{jp}), jet orifice diameter (D_j), counterflow velocity (U_C), and counterflow tube diameter (D_C). A compact mathematical description was developed using dimensional analysis. Peak jet length was a function of the diameter of the counterflow chamber, the ratio of jet to counterflow momentum $= \frac{U_{jp}^2 D_j^2}{U_c^2 D_c^2}$, and a previously undescribed jet pulsatility parameter, the pulsatility index (PI). $PI = \frac{D_c^2}{T_{jp} U_{jp} D_j}$. For the same jet orifice flow conditions, jet penetration decreased as chamber diameter decreased, as jet PI increased, and as the momentum ratio decreased. These interactions provide insight into why regurgitant jet size is not always a good estimate of regurgitant severity.

The noninvasive assessment of mitral regurgitation has been an elusive clinical goal. Recent studies have highlighted the value of pulmonary venous (PV) flow reversal in indicating the presence of severe regurgitation. The purpose of this study was to explore the basic determinants of PV inflow in the presence and absence of regurgitation. In particular, the hypothesis that PV flow reversal depends on the interaction of regurgitant volume with atrial and PV properties (compliance, initial volume, total area of the PVs at the atrial junction, and the inertia of PV inflow) was tested and further, that the combination of these variables, rather than regurgitant volume alone, determines PV inflow. A mathematical model of an atrium and PVs was developed. Atrial and PV pressure were each modeled as the product of chamber elastance and volume, where atrial elastance varied in time to simulate atrial relaxation and descent of the mitral annulus. A simplification of the modified unsteady Bernoulli equation was used to compute the PV velocities that result from the developed pressure gradient. The modeling was performed over a range of initial atrial elastances (0.77 - 0.2 mmHg/cc), initial atrial volumes (20 - 75 cc), total PV areas (3.12 - 5.12 cm^2), and PV inflow inertances (8 - 18 g/cm^2), with and without the addition of two regurgitant jets (regurgitant volume of 20 and 60 cc). The model realistically simulated the systolic PV wave form in magnitude and morphology. As the volume of regurgitation increased, PV peak flow velocity decreased, and eventually late systolic flow reversal occurred. However, the peak flow velocity, the time to peak flow, and the presence and magnitude of flow reversal were all influenced by atrial compliance, volume, total atrial inlet area, and PV inflow inertia. This study found that, PV flow blunting and reversal increased as atrial compliance, volume, and PV inertia decreased and as atrial inlet area increased. Atrial and PV properties (compliance, volume, total PV atrial inlet area, PV inflow inertia), acting in combination, mediate the physiologic impact of the regurgitant lesion in terms of the resulting rise in atrial pressure as reflected by the pattern of systolic PV influx. For example, PV flow reversal is more likely in acute compared to chronic regurgitation because the atrium is less compliant and has a smaller initial volume. Therefore, clinical assessments of mitral regurgitation using systolic PV flow reversal must be viewed in the context of atrial and PV properties.

PUBLICATIONS

1. Jain, S. P., Fan, P-H., Philpot, E. F., Nanda, N. C., Agrawal, K. K., and Yoganathan, A. P., "Influence of Various Instrument Settings on the Flow Information Derived from the Power Mode," ***Ultrasound in Medicine and Biology***, vol. **17**, pp. 49-54, 1991.

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SUBMITTED JOURNAL PAPERS

1. Grimes, R. Y., Hopmeyer, J., Cape, E. G., Yoganathan, A. P., and Levine, R. A., "Quantification of Mitral and Tricuspid Regurgitation Using Jet Centerline Velocities: An In Vitro Study of Jets in an Ambient Counterflow," ***Echocardiography***.

2. Grimes, R. Y., Hopmeyer, J., Cape, E. G., Levine, R. A. and Yoganathan, A. P., "How Sensitive are Jet Centerline Velocities to an Opposing Flow? Implications for Using the Centerline Method to Quantify Regurgitant Jet Flow," ***Journal of Biomechanics.***

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